AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions:

Listing of Claims:

- 1. (currently amended) A method of treating myelodysplastic syndromes, lymphomas and leukemias, and solid tumors in a mammal which comprises treating the mammal in need of such treatment simultaneously, concurrently, separately or sequentially with pharmaceutically effective amounts of (a) a FLT-3 inhibitor, or a pharmaceutically acceptable salt or a prodrug thereof, and (b) a histone deacetylase inhibitor (HDAI), or a pharmaceutically acceptable salt or a prodrug thereof.
- 2. (original) The method according to claim 1 for treating acute myeloid leukemia (AML).
- 3. (original) The method according to claim1, wherein the FLT-3 inhibitor is a staurosporine derivative.
- 4. (currently amended) The method according to claim 3, wherein the staurosporine derivative is selected from the compounds of formula,

$$(R_{1})_{m} \xrightarrow{g} \begin{array}{c} B \\ NR_{5} \\ NR$$

$$(R_{1})_{m} \xrightarrow{g} B \xrightarrow{10} B \xrightarrow{11} O \xrightarrow{R_{1}} (R_{2})_{n}$$

$$Z = O \xrightarrow{R_{2}} R_{6}$$

$$(R_{1})_{m} \xrightarrow{g} B \times 7 \xrightarrow{6} NR_{5} O \xrightarrow{4} \xrightarrow{3} (R_{2})_{n}$$

$$(CH_{2})_{m} \xrightarrow{(CH_{2})_{n}} R_{8}$$

$$(IV)$$

or or

$$(R_{1})_{m_{9}} = 8 \times 7 \times 7 \times 5 \times 10^{-10} \times 10^{-10}$$

wherein R₁ and R₂, are, independently of one another, unsubstituted or substituted alkyl, hydrogen, halogen, hydroxy, etherified or esterified hydroxy, amino, mono- or disubstituted amino, cyano, nitro, mercapto, substituted mercapto, carboxy, esterified carboxy, carbamoyl, N-mono- or N,N-di-substituted carbamoyl, sulfo, substituted sulfonyl, aminosulfonyl or N-mono- or N,N-di-substituted aminosulfonyl;

n and m are, independently of one another, a number from and including 0 to and including 4;

n' and m' are, independently of one another, a number from and including-1 to and including-4;

 R_3 , R_4 , R_8 and R_{10} are, independently of one another, hydrogen, an aliphatic, carbocyclic, or carbocyclic-aliphatic radical with up to 29 carbon atoms in each case, a heterocyclic or heterocyclic-aliphatic radical with up to 20 carbon atoms in each case, and in each case up to 9 heteroatoms, an acyl with up to 30 carbon atoms, wherein R_4 may also be absent;

or R₃ is acyl with up to 30 carbon atoms and R₄ not an acyl;

p is 0 if R_4 is absent, or is 1 if R_3 and R_4 are both present and in each case are one of the aforementioned radicals;

R₅ is hydrogen, an aliphatic, carbocyclic, or carbocyclic-aliphatic radical with up to 29 carbon atoms in each case, or a heterocyclic or heterocyclic-aliphatic radical with up to 20 carbon atoms in each case, and in each case up to 9 heteroatoms, or acyl with up to 30 carbon atoms;

R₇, R₆ and R₉ are acyl or –(lower alkyl) –acyl, unsubstituted or substituted alkyl, hydrogen, halogen, hydroxy, etherified or esterified hydroxy, amino, mono- or disubstituted amino, cyano, nitro, mercapto, substituted mercapto, carboxy,carbonyl, carbonyldioxy, esterified carboxy, carbamoyl, N-mono- or N,N-di-substituted carbamoyl, sulfo, substituted sulfonyl, aminosulfonyl or N-mono- or N,N-di-substituted aminosulfonyl;

X stands for 2 hydrogen atoms; for 1 hydrogen atom and hydroxy; for O; or for hydrogen and lower alkoxy;

Z stands for hydrogen or lower alkyl;

and either the two bonds characterised by wavy lines are absent in ring A and replaced by 4 hydrogen atoms, and the two wavy lines in ring B each, together with the respective parallel bond, signify a double bond;

or the two bonds characterised by wavy lines are absent in ring B and replaced by a total of 4 hydrogen atoms, and the two wavy lines in ring A each, together with the respective parallel bond, signify a double bond;

or both in ring A and in ring B all of the 4 wavy bonds are absent and are replaced by a total of 8 hydrogen atoms;

or a salt thereof, if at least one salt-forming group is present.

5. (original) The method according to claim 3, wherein the staurosporine derivative is a staurosporin derivative of formula I,

$$(R_1)_m$$
 $(R_1)_m$
 $(R_2)_m$
 $(R_3)_m$
 $(R_4)_m$
 $(R_2)_m$
 $(R_3)_m$
 $(R_4)_m$
 $(R_3)_m$
 $(R_3)_m$
 $(R_4)_m$
 $(R_3)_m$
 $(R_4)_m$
 $(R_3)_m$

wherein

m and n are each 0;

R₃ and R₄ are independently of each other

hydrogen,

lower alkyl unsubstituted or mono- or disubstituted, especially monosubstituted, by radicals selected independently of one another from carboxy; lower alkoxycarbonyl; and cyano; or

R₄ is hydrogen or -CH₃, and

R₃ is acyl of the subformula R°-CO, wherein R° is lower alkyl; amino-lower alkyl, wherein the amino group is present in unprotected form or is protected by lower alkoxycarbonyl; tetrahydropyranyloxy-lower alkyl; phenyl; imidazolyl-lower alkoxyphenyl; carboxyphenyl; lower alkoxycarbonylphenyl; halogen-lower alkylphenyl; imidazol-1-ylphenyl; pyrrolidino-lower alkylphenyl; piperazino-lower alkylphenyl; (4-lower alkylpiperazinomethyl)phenyl; morpholinolower alkylphenyl; piperazinocarbonylphenyl; or (4-lower alkylpiperazino)phenyl;

or is acyl of the subformula R°-O-CO-, wherein R° is lower alkyl;

or is acyl of the subformula R°HN-C(=W)-, wherein W is oxygen and R° has the following meanings: morpholino-lower alkyl, phenyl, lower alkoxyphenyl, carboxyphenyl, or lower alkoxycarbonylphenyl;

or R₃ is lower alkylphenylsulfonyl, typically 4-toluenesulfonyl;

R₅ is hydrogen or lower alkyl, X stands for 2 hydrogen atoms or for O; Z is methyl or hydrogen; or a salt thereof, if at least one salt-forming group is present.

6. (original) The method according to claim3, wherein the staurosporine derivative is N-[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H- diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-*N*-methylbenzamide of the formula (VII):

or a salt thereof.

7. (original) The method according to claim 1, wherein the HDAI compound is a histone deacetylase inhibitor of formula (X)

HO
$$R_1$$
 R_2 R_3 R_4 R_5 R_5 R_5 R_5 R_5

wherein

R₁ is H, halo, or a straight chain C₁-C₆ alkyl;

 R_2 is selected from H, C_1 - C_{10} alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, C_4 – C_9 heterocycloalkylalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, -(CH_2)_n $C(O)R_6$, -(CH_2)_n $OC(O)R_6$, amino acyl, HON-C(O)-CH=C(R_1)-aryl-alkyl- and - (CH_2)_n R_7 ;

 R_3 and R_4 are the same or different and independently H, C_1 - C_6 alkyl, acyl or acylamino, or R_3 and R_4 together with the carbon to which they are bound represent C=O, C=S, or C=NR₈, or R_2 together with the nitrogen to which it is bound and R_3 together with the carbon to which it is bound can form a C_4 – C_9 heterocycloalkyl, a heteroaryl, a

- polyheteroaryl, a non-aromatic polyheterocycle, or a mixed aryl and non-aryl polyheterocycle ring;
- R₅ is selected from H, C₁-C₆ alkyl, C₄ C₉ cycloalkyl, C₄ C₉ heterocycloalkyl, acyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, aromatic polycycle, non-aromatic polycycle, mixed aryl and non-aryl polycycle, polyheteroaryl, non-aromatic polyheterocycle, and mixed aryl and non-aryl polyheterocycle;
- n_1 , n_2 and n_3 are the same or different and independently selected from 0 6, when n_1 is 1-6, each carbon atom can be optionally and independently substituted with R_3 and/or R_4 ;
- X and Y are the same or different and independently selected from H, halo, C₁-C₄ alkyl, NO₂, C(O)R₁, OR₉, SR₉, CN, and NR₁₀R₁₁;
- R_6 is selected from H, C_1 - C_6 alkyl, C_4 C_9 cycloalkyl, C_4 C_9 heterocycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, OR_{12} , and $NR_{13}R_{14}$;
- R_7 is selected from OR_{15} , SR_{15} , $S(O)R_{16}$, SO_2R_{17} , $NR_{13}R_{14}$, and $NR_{12}SO_2R_6$;
- R_8 is selected from H, OR_{15} , $NR_{13}R_{14}$, C_1 - C_6 alkyl, C_4 C_9 cycloalkyl, C_4 C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;
- R_9 is selected from $C_1 C_4$ alkyl and C(O)-alkyl;
- R₁₀ and R₁₁ are the same or different and independently selected from H, C₁-C₄ alkyl, and C(O)-alkyl;
- R₁₂ is selected from H, C₁-C₆ alkyl, C₄ C₉ cycloalkyl, C₄ C₉ heterocycloalkyl, C₄ C₉ heterocycloalkylalkyl, aryl, mixed aryl and non-aryl polycycle, heteroaryl, arylalkyl, and heteroarylalkyl;
- R_{13} and R_{14} are the same or different and independently selected from H, C_1 - C_6 alkyl, C_4 C_9 cycloalkyl, C_4 C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, amino acyl, or R_{13} and R_{14} together with the nitrogen to which they are bound are C_4 C_9 heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle;
- R_{15} is selected from H, C_1 - C_6 alkyl, C_4 C_9 cycloalkyl, C_4 C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl and $(CH_2)_m ZR_{12}$;
- R_{16} is selected from C_1 - C_6 alkyl, C_4 C_9 cycloalkyl, C_4 C_9 heterocycloalkyl, aryl, heteroaryl, polyheteroaryl, arylalkyl, heteroarylalkyl and $(CH_2)_m ZR_{12}$;
- R_{17} is selected from C_1 - C_6 alkyl, C_4 C_9 cycloalkyl, C_4 C_9 heterocycloalkyl, aryl, aromatic polycycle, heteroaryl, arylalkyl, heteroarylalkyl, polyheteroaryl and $NR_{13}R_{14}$;
- m is an integer selected from 0 to 6; and
- Z is selected from O, NR₁₃, S and S(O);
- or a pharmaceutically acceptable salt thereof.
- 8. (original) The method according to claim 7, wherein each of R₁, X, Y, R₃, and R₄ is H.

- 9. (original) The method according to claim 8, wherein one of n_2 and n_3 is zero and the other is 1.
- 10. (original) The method according to claim 9, wherein one of n_2 and n_3 is zero and the other is 1.
- 11. (original) The method according to claim 1, wherein the histone deacetylase inhibitor is a compound of the formula (Xa)

HO N
$$R_2$$
 R_5 (Xa)

wherein

n₄ is 0-3,

 R_2 is selected from H, C_1 - C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, alkylcycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, -(CH_2)_n $C(O)R_6$, amino acyl and -(CH_2)_n R_7 ;

R₅' is heteroaryl, heteroarylalkyl, an aromatic polycycle, a non-aromatic polycycle, a mixed aryl and non-aryl polycycle, polyheteroaryl, or a mixed aryl and non-aryl polyheterocycle or a pharmaceutically acceptable salt thereof.

12. (original) The method according to claim 1, wherein the histone deacetylase inhibitor is a compound of the formula (Xb):

wherein

 R_2 ' is selected from H, C_1 - C_6 alkyl, C_4 - C_6 cycloalkyl, alkylcycloalkyl, and $(CH_2)_{2-4}OR_{21}$ where R_{21} is H, methyl, ethyl, propyl, or isopropyl, and

R₅" is unsubstituted or substituted 1*H*-indol-3-yl, benzofuran-3-yl or quinolin-3-yl or a pharmaceutically acceptable salt thereof.

13. (original) The method according to claim 1, wherein the histone deacetylase inhibitor is a compound of the formula (Xe)

HO N R1 R18 R18 N-R₂₀
$$R_1$$
 R_2 R_3 R_4 R_4 R_{20} R_4 R_{20} R_4 R_4 R_5 R_6 R_7 R_8 R_9 R_9

or a pharmaceutically acceptable salt thereof.

14. (previously presented) The method according to any one of claim 1, wherein the histone deacetylase inhibitor is selected from the group consisting of N-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, or, in each case a pharmaceutically acceptable salt thereof.

Claims 15-20 (cancelled).

- 21. (withdrawn) A pharmaceutical composition comprising (a) a FLT-3 inhibitor and (b) a histone deacetylase inhibitor for the treatment of myelodysplastic syndromes, lymphomas and leukemias and solid tumors.
- 22. (withdrawn) A pharmaceutical composition according to claim 21 for treating acute myeloid leukemia (AML), colorectal cancer (CRC) or non-small cell lung cancer (NSCLC).
- 23. (withdrawn) A pharmaceutical compositon according to claim 21, wherein the FLT-3 inhibitor is -[(9*S*,10*R*,11*R*,13*R*)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1*H*,9*H*-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-*N*-methylbenzamide of the formula (VII):

or a salt thereof and the HDAI is selected from the group consisting of N-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propenamide, or, in each case a pharmaceutically acceptable salt thereof.